INFLUENZA

✓DISEASE AND EPIDEMIOLOGY

Clinical Description:

Influenza is an acute respiratory disease characterized by fever, headache, myalgia (body aches), prostration, coryza (runny nose), sore throat, and cough. Recovery is usually rapid, but some patients may have lingering depression and asthenia (lack of strength or energy) for several weeks.

The most frequent complication of influenza is pneumonia, most commonly secondary bacterial pneumonia (e.g., *Streptococcus pneumoniae*, *Haemophilus influenzae*, or *Staphylococcus aureus*). Reye syndrome is a complication that occurs almost exclusively in children taking aspirin, primarily in association with influenza B (or varicella zoster [chickenpox]), and presents with severe vomiting and confusion, which may progress to coma due to swelling of the brain.

Causative agent:

Influenza is caused by RNA viruses from the *Orthomyxoviridae* family. There are three types of influenza viruses: A, B, and C. Influenza A viruses are further categorized by their H (hemagglutinin) and N (neurominidase) membrane glycoproteins.

Differential Diagnosis:

Viruses that cause symptoms similar to influenza include: respiratory syncytial virus (RSV), adenovirus, parainfluenza, and human metapneumovirus.

Laboratory identification:

Laboratory diagnosis of influenza is recommended when the prevalence of influenza disease is low (which is usually at the beginning or end of the influenza season), when a patient is severely ill with influenza-like symptoms and has no known risk factors for severe disease, and when other diseases that may cause influenza-like illness are known to be circulating in the community.

Culture:

Influenza virus culture is the gold standard for laboratory diagnosis. It has the advantage of being able to subtype influenza A viruses, but is time consuming and may not be appropriate when trying to determine treatment and prophylaxis. Appropriate clinical specimens include nasal washes, nasopharyngeal aspirates, nasal and throat swabs, transtracheal aspirates, and bronchoalveolar lavage. Specimens should be taken within 72 hours of onset of illness.

PCR:

PCR testing is a rapid way to diagnose infection, but it is also expensive and not widely available. It cannot subtype influenza A viruses.

DFA:
DFA testing detects the influenza virus directly from clinical samples. It is a rapid test with fairly good sensitivity and specificity. However, it can't subtype influenza A viruses.

Serology:
Because most human sera contain antibodies to influenza, diagnosis of influenza cannot be made from a single serum sample. The acute-phase specimen should be taken less than 5 days from onset, and a convalescent specimen taken 10–21 days (preferably 21 days) following onset. Serologic diagnosis of influenza is not accepted for the purposes of national surveillance due to a lack of standardized testing methods and interpretation.

Rapid Tests:
Rapid diagnostic testing for influenza antigen permits those in office and clinic settings to assess the need for antiviral use in a timelier manner. Currently available test kits fall into three groups; the first detects only influenza type A viruses, while the second detects both influenza type A and B viruses but does not differentiate between virus types, and the third detects both influenza type A and B viruses and distinguishes between the two. When interpreting results of a rapid influenza test, the level of influenza activity in the community should be considered. When influenza prevalence is low, positive rapid test results should be independently confirmed by culture or PCR.

Treatment:
Four licensed influenza antiviral agents are available in the United States: amantadine, rimantadine, zanamivir, and oseltamivir. Because antiviral testing results indicated high levels of resistance, neither amantadine nor rimantadine should be used for the treatment or chemoprophylaxis of influenza in the United States.

Antivirals require pre-authorization under Medicaid in ordinary circumstances. At each elevation of the influenza activity level, UDOH will consider requesting that Medicaid suspend this requirement.

Zanamivir and oseltamivir are active against both influenza type A and type B. Zanamivir is approved for treatment of uncomplicated acute influenza A or B in persons 7 years of age and older. Oseltamivir is approved for the treatment of uncomplicated influenza A or B in persons 1 year of age and older. Treatment of influenza with antivirals should start as soon as possible, but within 48 hours of disease onset for maximum reduction in symptom severity and duration. Information on dosage and routes of administration can be found at: http://www.cdc.gov/flu/professionals/treatment/index.htm

Aspirin should not be used for infants, children, or teenagers because they may be at risk for contracting Reye syndrome following an influenza infection.

Case fatality:
Influenza, by itself, is rarely fatal. However, people in high-risk categories are subject to secondary infections that can be life threatening. Death is reported in 0.5–1 per 1,000 cases. The majority of deaths occur among persons 65 years of age and older.

Reservoir:
Humans are the only known reservoir of influenza types B and C. Influenza A may infect humans, birds (predominantly poultry) and mammals (such as swine).

Transmission:
Influenza is primarily transmitted via large droplets generated when infected persons cough or sneeze. Transmission may also occur through direct contact or indirect contact with respiratory secretions such as when touching surfaces contaminated with influenza virus and then touching the eyes, nose or mouth. The virus has good persistence in the environment. Attack rates range from 10-20% in the general population, but can be as high as 50% in closed populations such as nursing homes.

Susceptibility:
All humans are thought to be susceptible to influenza, although certain high-risk populations are more likely to suffer from severe illness or death.

Adults categorized as being at high risk for influenza-related complications:

- Told by a physician they had diabetes, weak or failing kidneys, coronary heart disease, angina, heart attack, or other heart condition
- Having a diagnosis of cancer during the previous 12 months (excluding nonmelanoma skin cancer) or ever being told by a physician they have lymphoma, leukemia, or blood cancer during the previous 12 months
- Told by a physician they have chronic bronchitis or emphysema, or report having an asthma episode or attack during the preceding 12 months

Children aged <18 years categorized as being at high risk for influenza-related complications:

- Told by a physician they had diabetes, sickle cell anemia, congenital heart disease, other heart disease
- Told by a physician they had neuromuscular conditions (seizures, cerebral palsy, and muscular dystrophy)
- Told by a physician they had cystic fibrosis, or report having an asthma episode or attack during the preceding 12 months

Because of the variability of the virus, infection does not produce immunity. Influenza activity peaks from December to March in temperate climates, but may occur earlier or later.

Incubation period:
Influenza has a short incubation period, typically 1-3 days.

Period of communicability:
In adults, influenza is transmissible from 1 day before symptom onset until 5 days after onset. Children can transmit the virus 10 or more days after symptom onset. Immunocompromised persons can shed virus for weeks to months after infection.

Epidemiology:

Antigenic drift, which occurs in all three types of influenza virus, is a minor change in surface antigens that results from point mutations in a gene segment. Influenza viruses are constantly undergoing antigenic drift. Because the virus is constantly making small changes, yearly vaccinations are necessary to provide protection to the different viruses.

Antigenic shift, which occurs only in influenza A viruses, is a major change in one or both surface antigens (H or N) that occurs at varying intervals. Antigenic shifts are probably due to genetic recombination (an exchange of a gene segment) between influenza A viruses, usually those that affect humans and birds. An antigenic shift may result in a worldwide pandemic if the virus is efficiently transmitted from person to person. There is concern that the increasingly wide geographic distribution of avian influenza (H5N1) could increase the chance of another antigenic shift.

The risk for complications and hospitalizations from influenza are higher among persons 65 years of age and older, young children, and persons of any age with certain underlying medical conditions. An average of more than 200,000 hospitalizations per year are related to influenza.

✓PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

Public health tracks the timing, magnitude, and severity of the annual epidemic through several surveillance systems:

- Influenza-associated hospitalizations
- Pediatric influenza-associated deaths
- School absenteeism
- Sentinel clinic influenza-like illness (ILI) reporting
- Laboratory testing

Prevention:

The primary method to prevent influenza infection is yearly vaccination. “Respiratory etiquette” is another way to prevent infection, and includes:

- Staying away from people who are sick and staying away from other people when you are sick. Don’t go to work, school, church, or other places where people gather if you are sick.
- Covering your mouth and nose when you cough or sneeze. Use a disposable tissue and throw it away when you are done.
- Washing your hands with soap and warm water, or use alcohol-based hand sanitizers, frequently.

Chemoprophylaxis:

Oseltamivir and zanamivir can be used for chemoprophylaxis of influenza; oseltamivir is licensed for use as chemoprophylaxis in persons aged >1 year, and zanamivir is licensed for use in persons aged >5 years.
Prophylaxis is recommended for prevention of disease in:

- Persons who have been vaccinated for less than two weeks.
- Unvaccinated people caring for those at high risk (employees of hospitals, clinics, or chronic-care facilities, household members, visiting nurses or volunteers.
- People with immune deficiencies or those who might not respond to vaccination (this includes persons infected with HIV or receiving immunosuppressive medications.)
- People who cannot receive influenza vaccine due to an egg allergy or other contraindication.
- Anyone exposed to influenza who does not want to develop disease.

Vaccine:

Two types of influenza vaccine are available in the United States. The vaccines are composed of three different types of influenza viruses: a type A (H1N1), a type A (H3N2), and a type B. The formulation changes every year to account for differences in the strains circulating.

Trivalent inactivated influenza vaccine (TIV) has been available since the 1940s. TIV is approved for use in anyone 6 months of age or older, regardless of the presence of chronic illness. TIV is administered by the intramuscular route.

Live attenuated influenza vaccine (LAIV) was approved for use in the United States in 2003. LAIV is approved for healthy, nonpregnant persons aged 2-49 years. LAIV is administered by the intranasal route.

All children aged ≥6 months - 8 years who have not been vaccinated previously at any time with either LAIV or TIV should receive 2 doses of vaccine in the same season, with a single dose during subsequent seasons. All other persons should receive on dose.

Annual vaccination is recommended for:

- All persons, including school-aged children, who want to reduce the risk of becoming ill with influenza or of transmitting influenza to others
- All children aged 6–59 months (i.e., 6 months–4 years);
- All persons aged >50 years;
- Children and adolescents (aged 6 months–18 years) receiving long-term aspirin therapy who therefore might be at risk for experiencing Reye syndrome after influenza virus infection;
- Women who will be pregnant during the influenza season;
- Adults and children who have chronic pulmonary (including asthma), cardiovascular (except hypertension), renal, hepatic, hematological or metabolic disorders (including diabetes mellitus);

- Adults and children who have immunosuppression (including immunosuppression caused by medications or by human immunodeficiency virus;
- Adults and children who have any condition (e.g., cognitive dysfunction, spinal cord injuries, seizure disorders, or other neuromuscular disorders) that can compromise respiratory function or the handling of respiratory secretions or that can increase the risk for aspiration;
- Residents of nursing homes and other chronic-care facilities;
- Health-care personnel;
- Healthy household contacts (including children) and caregivers of children aged <5 years and adults aged >50 years, with particular emphasis on vaccinating contacts of children aged <6 months; and
- Healthy household contacts (including children) and caregivers of persons with medical conditions that put them at higher risk for severe complications from influenza.

When vaccine supplies are limited, vaccination should be encouraged in high-risk populations that are at greater risk of severe disease or death.

Isolation and quarantine requirements:

Isolation: NA

Hospital: Hospitals should follow droplet precautions for five days unless the patient is immunocompromised, in which droplet precautions should be followed for the duration of illness.

Quarantine: NA

✓CASE INVESTIGATION

Reporting:

Influenza-associated hospitalizations are a reportable disease in Utah. Influenza-associated pediatric mortality is a reportable disease, both nationally and in Utah.

Additional investigation may be warranted in the event that someone is diagnosed with influenza and has a recent travel history to an area with current avian influenza activity, regardless of hospitalization. The person should be contacted to determine the nature of their visit and any possible exposures. If a possible exposure occurred, a nasopharyngeal *and* an oropharyngeal sample should be sent to UPHL for H5N1 testing. UPHL should be contacted and made aware of the situation and notified that a sample is being sent for H5N1 testing. UPHL may still decide to test for H5N1 even if no exposure occurred, and therefore should be notified when any influenza case with a recent travel history is identified.

Case Definition:

Influenza-associated hospitalization:

Case Classification

Probable: A hospitalized case of influenza that has been diagnosed via rapid test or single serum serology.

Confirmed: A hospitalized case of influenza that has been diagnosed via culture, PCR, DFA, or a four-fold rise in paired acute and convalescent sera.

Influenza-associated pediatric mortality (2004):

Case Definition

An influenza-associated death is defined for surveillance purposes as a death resulting from a clinically compatible illness that was confirmed to be influenza by an appropriate laboratory or rapid diagnostic test. There should be no period of complete recovery between the illness and death. Influenza-associated deaths in all persons aged <18 years should be reported.

A death should not be reported if:

1. There is no laboratory confirmation of influenza virus infection.
2. The influenza illness is followed by full recovery to baseline health status prior to death.
3. The death occurs in a person 18 years or older.
4. After review and consultation there is an alternative agreed upon cause of death.

Laboratory Criteria

Laboratory testing for influenza virus infection may be done on pre- or post-mortem clinical specimens, and include identification of influenza A or B virus infections by a positive result by at least one of the following:

- Influenza virus isolation in tissue cell culture from respiratory specimens;
- Reverse-transcriptase polymerase chain reaction (RT-PCR) testing of respiratory specimens;
- Immunofluorescent antibody staining (direct or indirect) of respiratory specimens;
- Rapid influenza diagnostic testing of respiratory specimens;
- Immunohistochemical (IHC) staining for influenza viral antigens in respiratory tract tissue from autopsy specimens;
- Four-fold rise in influenza hemagglutination inhibition (HI) antibody titer in paired acute and convalescent sera.

Case Classification

Confirmed: A death meeting the clinical case definition that is laboratory confirmed.

Laboratory or rapid diagnostic test confirmation is required as part of the case definition; therefore, all reported deaths will be classified as confirmed.

Comment

Serologic testing for influenza is available in a limited number of laboratories, and should only be considered as evidence of recent infection if a four-fold rise in influenza (HI) antibody titer is demonstrated in paired sera. Single serum samples are not interpretable.

Case Investigation Process:

Hospital infection control practitioners play a crucial role in Utah's influenza-associated hospitalization reporting system, and most cases are first identified through ICPs. Cases of Utah's influenza-associated hospitalizations should be managed as follows:

- Confirmatory laboratory testing should be performed. If a case is initially diagnosed via rapid, UDOH strongly recommends confirmation by culture. UPHL can provide confirmation, and can use the residual eluate on a nasopharyngeal swab that is left over from certain rapid influenza tests.

As part of Utah's system to detect pediatric influenza-associated deaths, the Office of the Medical Examiner (OME) tests for influenza virus on all pediatric deaths with compatible symptoms. Therefore, most pediatric influenza-associated deaths are identified first through the OME. Whether a case is classified as a pediatric influenza-associated death takes into account hospitalization records, medical history, the autopsy report, and the case classification. Because autopsy reports can take several months to complete, the process is not timely and cases are not used to evaluate the influenza season. Pediatric influenza-associated deaths should be managed as follows:

- UDOH epidemiology staff will send a fax to the OME requesting demographic data on the patient and the completed autopsy report.
- Once the residence of the case is known, the local health department will be notified.
- The local health department will usually investigate as much as they can through hospitalization records.
- The OME will fax UDOH epidemiology the final autopsy report, which will be forwarded on to the local health department, and public health will decide whether the case can be classified as a pediatric influenza-associated death.

Outbreaks:

A state-wide outbreak effectively occurs every year during influenza season when influenza-like illness levels increase above threshold. General measures to control activity during influenza season include vaccination, respiratory etiquette, and staying home when sick.

However, localized outbreaks can occur, and may require additional intervention from public health. Outbreaks of healthcare-associated influenza can occur and affect both patients and personnel in long-term care facilities and hospitals. The following documents were developed by CDC to guide infection control measures for outbreaks in institutional and acute-care facilities.

- Infection Control Measures for Preventing and Controlling Influenza Transmission in Long-Term Care Facilities

- Infection Control Guidance for the Prevention and Control of Influenza in Acute-Care Facilities

School, particularly daycare and elementary, outbreaks can occur and can spread very quickly because of close contact and decreased hygiene habits of younger children. In some situations, schools have had to close because of the high number of absences in students and teachers. Teaching children appropriate hygiene and respiratory etiquette and instituting isolation policies for sick children during influenza season can help control the spread of disease.

Identification of case contacts:

Contacts of influenza cases are usually not traced. Certain situations may warrant contact tracing, such as a novel influenza virus strain, exposure in a setting with substantial high-risk contacts, or certain outbreaks. The decision to track case contacts should be made by public health and should follow CDC guidelines.

Case contact management:

In the event that case contacts are tracked, management should follow CDC guidelines.

✓REFERENCES

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